study was shown to be superior to those of Celecoxib for treating active osteoarthritis.

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A PILOT STUDY OF THE USE OF A TRUFIT PLUG FOR CARTILAGE REPAIR IN THE KNEE AND HOW TO DEAL WITH EARLY CLINICAL FAILURES?

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Purpose: The purpose of this pilot study is to present our short-term experience with the TruFit plug (Smith & Nephew, Andover, MA) for cartilage repair in the knee and to discuss our approach to treat early clinical failures.
Methods: Twenty patients were consecutively treated for their cartilage lesion with this plug technique. These patients were prospectively clinically evaluated at 6 and 12 months of follow-up. Magnetic resonance imaging (MRI) was used for morphological analysis of the cartilage repair. Biopsy samples were taken from 3 cases during revision surgery, allowing histological assesment of the repair tissue.
Results: The short-term clinical and MRI outcome of this pilot study are mediocre. No signs of deterioration of the repair tissue were observed. Three of the 15 patients (20.0%) displayed persistent or even more clinical symptoms after insertion of the plug. These patients were considered as failures and therefore eligible for revision surgery. During revision surgery the repair tissue was carefully removed. The remaining osteochondral defect was filled with autologous bone grafts. Immediate and persistent relieve of symptoms was observed in all 3 patients. Histological assessment of biopsy specimens taken during revision surgery of these 3 patients revealed fibrous vascularized repair tissue with the presence of foreign-body giant cells.
Conclusion: The overall short term clinical and MRI outcome of a TruFit plug for cartilage repair in the knee is mediocre. In this pilot study a modest clinical improvement became apparent at 12 months of follow-up. MRI data showed no deterioration of the repair tissue. Remarkably, 3 of the 15 patients (20%) had persistent clinical symptoms after surgery. These patients were succesfully treated with the removal of the osteochondral plug remnants and the application of autologous bone grafts. Longer follow-up studies and randomised controlled trials are mandatory to confirm the findings of this pilot study.

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MID-TERM RESULTS OF THE TREATMENT OF CARTILAGE DEFECTS IN THE KNEE USING ALGINATE BEADS CONTAINING HUMAN MATURE ALLOGENIC CHONDROCYTES

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Purpose: The purpose of this paper was to present our mid-term experience with the implantation of alginate beads containing human mature allogenic chondrocytes for the treatment of cartilage lesions in the knee.
Methods: A biodegradable, alginate-based biocompatible scaffold containing human mature allogenic chondrocytes was used for cartilage lesions in the knee. Twenty-one patients were clinically prospectively evaluated with use of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and a Visual Analogue Scale (VAS). The mean follow-up time was 6.3 years (5–8 years). MRI data were analyzed based on the MOCART (Magnetic Resonance Observation of Cartilage Repair Tissue) system, allowing morphological assessment of the repair tissue. MRI images were taken at one year of follow-up and at a mean follow-up of 6.1 years (5–7 years).
Results: During the follow-up period the WOMAC and VAS scores improved significantly. No signs of clinical deterioration or adverse reactions to the alginate beads/allogenic chondrocyte implantation were observed. Four failures occured during the follow-up period in this study (19.05%). The MOCART scoring methods indicated that the condition of the repair tissue deteriorated on MRI.
Conclusions: This investigation provided useful information on the efficacy of this new treatment in chondral lesions of the knee. The mid-term clinical outcome of the presented technique was promising. However, these results were not confirmed by the MRI findings. Moreover, the MRI data indicated a deterioration of the repair tissue. These results inspire us to search for further improvements of this technique.

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DULOXETINE AS TREATMENT FOR KNEE PAIN IN PATIENTS WITH OSTEOARTHRITIS WHO REGULARLY USE NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs): A POST HOC ANALYSIS OF TWO RANDOMIZED, PLACEBO-CONTROLLED TRIALS

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Purpose: To examine whether treatment with duloxetine has similar efficacy in patients with symptomatic knee osteoarthritis (OA) who regularly use NSAIDs as compared with those who do not.
Methods: We conducted a post hoc analysis of data from 2 randomized, placebo-controlled trials of duloxetine in patients with symptomatic knee OA. In each trial, patients were randomized to 13 weeks of treatment with duloxetine 60–120 mg once daily or placebo, and stratified according to concomitant NSAID use at baseline. NSAID users were identified as those patients who were taking a therapeutic dose of NSAID or acetaminophen for ≥14 days per month for 3 months immediately preceding the study. Efficacy measures were the Brief Pain Inventory (BPI) 24-h average pain severity score (0–10), and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC;0–96). Missing data were imputed using last-observation-carried-forward method. Differences in treatment effect of duloxetine versus placebo between subgroups were analyzed with an ANCOVA model that included therapy, study, baseline value, concomitant NSAID use, and therapy-by-NSAID subgroup interaction. Safety and tolerability were assessed with spontaneously reported treatment-emergent adverse events (TEAEs).
Results: There were a total of 105 duloxetine NSAID users, 112 placebo NSAID users, 134 duloxetine non-NSAID users, and 136 placebo non-NSAID users. Overall mean baseline ratings were BPI average pain=6.15, and WOMAC total=51.37, and there were no significant differences between NSAID subgroups on these measures. Mean changes from baseline are summarized in Figure 1. Treatment-by-NSAID use interactions were not significant for either of the outcome measures, which suggests that the effect of duloxetine treatment was not affected by concomitant NSAID use. Nausea was the most common TEAE reported in patients treated with duloxetine vs. placebo that was significantly ($p < 0.05$) more frequent regardless of concomitant NSAID use. In addition among NSAID users, patients treated with duloxetine vs. placebo reported significantly more hyperhidrosis ($p < 0.05$); and constipation ($p < 0.01$) was reported significantly more frequently among the non-NSAID users.

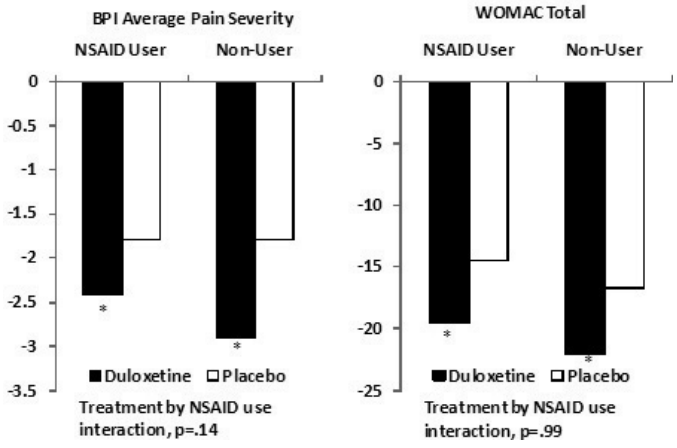

Fig. 1. Mean changes from baseline in BPI average pain severity and WOMAC total.

Conclusions: There were a total of 105 duloxetine NSAID users, 112 placebo NSAID users, 134 duloxetine non-NSAID users, and 136 placebo non-NSAID users. Overall mean baseline ratings were BPI average pain=6.15, and WOMAC total=51.37, and there were no significant differences between NSAID subgroups on these measures. Mean changes from baseline are summarized in Figure 1. Treatment-by-NSAID use interactions were not significant for either of the outcome measures, which suggests that the effect of duloxetine treatment was not affected by concomitant NSAID use. Nausea was the most common TEAE reported

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COMPARISON OF DIFFERENT EXPERIMENTAL DESIGNS TO EVALUATE THE EFFICACY OF AN INTERVENTION IN OSTEOARTHRITIS PATIENTS

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Purpose: The design of a clinical trial to test the efficacy of an intervention in osteoarthritis patients is strongly hampered by different factors such as the absence of a fully validated biomarker, the magnitude of the placebo effect and the enormous variability associated to the clinical outcomes. The objective of this study is to compare the validity and usefulness of different clinical trial designs to test the efficacy and safety of a food supplement for the management of knee osteoarthritis.
Methods: In order to study the effect of the trial design on the results achieved, 2 clinical trials testing the same product for the management of osteoarthritis (Hyal-Joint®, Bioiberica, Spain), have been compared. The first clinical trial (n = 71) used retrospective data from consecutive patients fulfilling inclusion criteria (moderate to severe knee OA coursing with synovitis) who were treated with Hyal-Joint (80 mg/d) or acetaminophen (500 mg/d). The second trial used the same sample size (n = 70) and same inclusion criteria, but the study was prospective and compared the treatment with Hyal-Joint (80 mg/d) or with placebo (80 mg/d) in a double-blind design. Progression of pain intensity (Huskisson's VAS) has been used as one of the clinical outcomes in both trials. Data from a subsequent prospective double-blind placebo-controlled clinical trial (n = 40) using alternative clinical outcomes has also been discussed. In this trial, instead of using traditional clinical outcomes such as pain perception, joint function was evaluated using standard isokinetic assessment (Biodex system 3 for measuring maximal muscle strength, total work and power mean).
Results: Results from the retrospective trial showed a 49.1% pain reduction from basal values after 3 months of treatment with Hyal-Joint, while the reduction associated to the treatment with acetaminophen was only of 23.1%. Differences between treatment groups were statistically significant ($P < 0.05$). Results from the prospective trial showed the same pain reduction from the basal values associated to the treatment with Hyal-Joint during 3 months (47.9%), but the reduction associated to the placebo treatment was of 39.6%, and differences between treatments groups only tended to reach statistical significance ($P > 0.05$). Interestingly, the pain relief associated to the placebo treatment is statistically higher than pain relief associated to acetaminophen ($P < 0.05$). On the subsequent clinical trial, statistically significant improvements were obtained compared to the placebo group even using a lower sample size (n = 40). The increase of the maximum peak torque of the knee extensors at 3 months compared to baseline was 6.5 ± 5.8 Nm for the active group and -1.0 ± 7.1 Nm for the placebo group at 240°/s ($P < 0.05$). The same pattern of response was obtained for total work ($P = 0.0588$) and power mean ($P < 0.05$).
Conclusions: The overall results show that variability of traditional clinical outcomes and the size of the placebo effect could difficult the obtaining of statistical results in osteoarthritis trials. According to the results, one possible strategy to overcome these handicaps could be the use of purely objective data such as the isokinetic assessment of the affected joint.

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LONG-TERM EFFICACY OF SEQUENTIALLY PROGRAMMED MAGNETIC FIELD (SPMF) THERAPY IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE

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Purpose: A study to demonstrate the efficacy of SPMF therapy on 195 patients (390 knees) with clinically and radiologically confirmed osteoarthritis (OA) of the knee, was published in the Scientific Medicine journal in 2009. The results showed an increase in cartilage thickness measured using MRI at three months follow-up compared to pre-treatment values**.** The present follow-up study was conducted, using the Knee Society clinical rating system, to demonstrate the long-term efficacy of SPMF, on varying grades of severity of OA.
Methods: This study was designed to be a prospective non-randomised clinical evaluation of SPMF therapy.
SPMFs are non-thermal and non-ionising electromagnetic fields, working on the principle of altering cell membrane potential by generating piezo-electric stimulus, resulting in cartilage and bone regeneration. When these fields are precisely focused on the tissues, they aid in regeneration of cartilage by the amplification of IGF-1, synthesis of proteoglycan, normalisation of the electromagnetic fileds in and around the Centrioles, and 'up-regulation' of HSR/HSF-1 pathways.
175 patients aged 30 years and above, with Grade III/IV OA (Kellgren & Lawrence grading system) of the knee, who had undergone SPMF therapy 9 months earlier were enrolled after obtaining their written consent.
The 9-month follow-up data were collected along the lines of previously collated pre-treatment and follow-up data. The main outcome measures included differences in pre-treatment parameters compared to the outcomes after SPMF therapy at intervals of 21 days, and 3 months and 9 months after completion of the therapy. Additionally, adverse effects to treatment were also recorded at 9-month follow-up.
Results: Statistical analysis of the collected data demonstrated an improvement in TFS scores from 39.64 (SD = 21.53) pre-treatment to 47.84 (SD = 18.54) at 21 days, 56.92 (SD = 16.47) at 3 months, and 61.20 (SD = 16.63) at 9 months follow-up.
The TKS score was 53.08 (SD = 17.39) at pre-treatment, which improved to 73.44 (SD = 13.61), 78.64 (SD = 12.26), and 83.32 (SD = 11.63) at 21 days, 3 months, and 9 months, respectively.
Participants with grade III OA showed an improvement in TFS from a pre-treatment score of 48.50 (SD = 33.46) to scores of 57.25 (SD = 23.25), 65.13 (SD = 21.02), and 71.62 (SD = 20.13) at 21 days, 3 months, and 9 months, respectively. For grade IV OA, the TFS score of 35.47 (SD = 12.15) pre-treatment, improved to 43.41 (SD = 14.63), 53.06 (SD = 12.80), and 56.29 (SD = 12.55) at 21 days, 3 months, and 9 months follow-up, respectively.
TKS scores for grade III OA improved from 63.63 (SD = 23.08) pre-treatment, to 78.62 (SD = 13.39), 83.87 (SD = 12.83) and 87.50 (SD = 14.28) at 21 days, 3 months, and 9 months follow-up, respectively. Similarly, the TKS scores for grade IV OA increased from 48.12 (SD = 11.78) pre-treatment to 71.00 (SD = 13.39), 76.17 (SD = 11.55), and 81.35 (SD = 10.04) at 21 days, 3 months and 9 months, respectively.
Conclusions: This study proves that SPMF therapy is an effective treatment modality for OA of the knee, as demonstrated through significant improvements in TKS and TFS scores at 21 days, 3 months and these scores are maintained over the follow up period of 9 months. In addition, the study also provides evidence to indicate that SPMF therapy improves outcomes in all grades of OA. This therapy should be a first line of treatment for OA due to its non-invasive nature, long term efficacy and since it can be provided on an out-patient basis.

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THE PRELIMINARY REPORT OF ENHANCED ROLE OF PLATELET-RICH PLASMA (PRP) WITH ARTHROSCOPIC MICROFRACTURE IN EARLY-STAGED OSTEOARTHRITIS OF KNEE

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Purpose: Platelet-Rich Plasma (PRP) is a natural concentrate of autologous blood growth factors experimented in different fields of medicine in order to test its potential to enhance tissue regeneration, and so was emerged as a treatment option for tendinopathies and chronic wounds. In addition to release of growth factors, PRP also promotes concentrated anti-inflammatory signals including interleukin-1a, which has been known to be a focus of emerging treatments for osteoarthritis. In cartilage defect of knee, arthroscopic microfracture is the most widely utilized cartilage restoration technique worldwide, and the results for most osteoarthritis patients are good, especially in the short term. However, according to many reports about this technique, the results of arthroscopic microfracture were not good in the patients of larger defects (>4 cm^2), older patients (age >40 years), and these factors likely influence on an overall observation that the results of microfracture tend to deteriorate over time, particularly after 2 years. Our authors suggested that the tissue-regenerative property of PRP can be helpful for enhancing the effect of the microfracture, but no references about this theory were found. The primary objective is to study the application of PRP with